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# AN EPIDEMIC OF APPENDICITIS AND PAROTITIS PROBABLY DUE TO STEPTOCOCCI CON- TAINED IN DAIRY PRODUCTS\*

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The occurrence of appendicitis in epidemic form, its seasonal prevalence, and its occurrence in several members of the same family have been noted repeatedly (Mantle,<sup>1</sup> Hood,<sup>2</sup> Martin,<sup>3</sup> Wahle,<sup>4</sup> Haim<sup>5</sup> and Rostouzew<sup>6</sup>).

The epidemic of appendicitis and parotitis studied by us occurred at the Culver Military Academy, Culver, Ind. The study was made at the request of the superintendent of the academy, Lieut.-Col. L. R. Gignilliat, to whom we wish to express our appreciation for the opportunity and also to Dr. C. E. Reed for much aid in the work. From February 21 to March 5, 1915, a period of 12 days, there occurred 8 cases of acute appendicitis; 2 cadets developing appendicitis on the same day. Seven of the 8 patients were operated on and the diagnosis verified. All recovered. Only 7 cases developed during the rest of the school year—2 in October, 1 in January, 3 in April, and 1 in May.

Two cadets developed parotitis previous to the sudden outbreak of appendicitis; 5 during the prevalence of appendicitis; 27 during March and April, and 3 in May, making a total of 34 cases. From April 10 to 18 there occurred an average of 1 new case a day and on April 25 3 students developed the disease. During the epidemic of parotitis 3 cadets developed appendicitis. The parotitis was not limited to the cadets, whose ages ranged from 15 to 19 years, but occurred in several older individuals as well.

The occurrence, the character, the duration, and the complications of the parotitis were typical. The epidemics occurred without associated tonsillitis. The cases of appendicitis were so distributed among the population as to rule out the factor of trauma from violent exercise.

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<sup>1</sup> Lancet, 1910, 2, p. 57.

<sup>2</sup> Ibid., 1, p. 1645.

<sup>3</sup> München. med. Wchnschr., 1912, 59, p. 2005.

<sup>4</sup> Ibid., p. 1438.

<sup>5</sup> Arch. f. klin. Chir., 1907, 82, p. 360.

<sup>6</sup> Mitt. a d. Grenzgeb. d. Med. u. Chir., 1906, 15, p. 564.

The total number of persons at the academy who ate in a common dining room of the same food was approximately 500. Of these, 430 were cadets, ranging in age from 15 to 19 years; 30 were members of the faculty; 40 were helpers, having to do with the preparation and serving of the food, etc. The sanitary conditions, the refrigerating plant, the kitchen and dining-room, the quality of food served, the method of handling food, the mode of life as to exercise, etc., and the general physique and health of the cadets were all found to be excellent.

The dairy products consumed were obtained from 4 independent sources. The milk and cream and the ice cream served at the mess were from a number of dairies directly under the supervision of the authorities at the academy. These dairies were kept in first-class condition, and the milk was cooled soon after milking, and refrigerated continuously until used. The butter, of first-grade quality, was an Indiana product from a neighboring town. The cheese was from southern Wisconsin. The ice cream served to many cadets at a neighboring shop was found to be prepared from unpasteurized cream obtained from local dairies under unsanitary surroundings and with deficient refrigeration.

Since virulent streptococci have been isolated frequently from the udders of cows with mastitis, and even from normal udders in model dairies (Rosenow<sup>9</sup>), and since epidemics of septic sore throat, scarlet fever, and typhoid fever have been traced to milk, the possibility that the outbreaks under consideration were due to bacteria in the dairy products had to be considered. Cultures and animal inoculations were therefore made of the milk, cream, butter, and cheese which were for general consumption at the mess, and of the ice cream which was consumed by the cadets at the neighboring shop. A similar study was also made of cultures obtained from the tonsils of cadets, of members of the corps who prepared and served the food, of members of the faculty, and of those that developed appendicitis.

#### TECHNIC

The technic of making cultures and animal inoculations was similar to that described in connection with the production of appendicitis.<sup>7</sup> Material for the cultures in the cases of parotitis was obtained from Steno's duct of the involved gland by catheterization and from the tonsils. An attempt was made to obtain material from the depth of the tonsils and not merely by swabbing the surface. The sediment of from 50 to 200 c.c. of milk and cream was used for the inoculations of the media. The butter and the cheese

<sup>7</sup> Jour. Infect. Dis., 1915, 16, p. 240.

(approximately 0.5 c.c.), obtained in a sterile manner from the depth of a freshly cut surface of the original package, were emulsified in 2 c.c. of NaCl solution and then planted.

The bacteriologic study consisted in the main of making blood-agar-plate cultures and inoculations of the material to be examined into a series of tall columns of ascites (10%) dextrose (0.2%) broth. These were incubated at 37 C. over night; then the character of the growth on the plates was noted and smears of the cultures in broth were made; those cultures in which no bacilli or only a few were found, were used for intravenous injection into rabbits and dogs. The bacteria for these injections were suspended in salt solution so that 1 c.c. contained the growth from 15 c.c. of the broth culture. A portion of the suspension injected was again plated on blood agar. The animals, often injected in series with doses ranging from 1 to 6 c.c., were chloroformed usually in 48 hours, if they had not already died from the effects of the injection. The examinations were made as soon after death as possible. The organism responsible for the lesions was determined by culture and from sections.

#### RESULTS OF INVESTIGATION

Sections from 4 of the human appendices, all showed streptococci, some in almost pure growth. In the case of one patient cultures were made both from the tonsils and from the wall of the appendix. That from the tonsils showed a predominating number of short-chained, green-producing streptococci, a few hemolytic streptococci, and a moderate number of *Micrococcus catarrhalis*; those from the wall of the appendix showed colon bacilli and green-producing streptococci. The culture in ascites dextrose broth from the tonsils of this patient was injected into 3 rabbits. All remained well and none showed lesions in the appendix. The growth from the appendix wall produced lesions in the appendix in 2 of 4 rabbits.

The findings in the case of another patient further illustrate the results obtained:

M., a cadet who developed symptoms of acute appendicitis on February 21, was operated upon on the following day and the acutely inflamed and edematous appendix removed. The lumen of this appendix was found to be very narrow and filled with bloody pus. There was no fecal concretion or other foreign body, and there were no constricting bands. The peritoneal coat was edematous and opaque and over the portion near the distal end was a thin fibrinous exudate. The mucous membrane was edematous and hemorrhagic throughout the larger portion, this condition extending well into the submucosa and the peritoneal coat. Sections showed an enormous number of streptococci within the lumen and within the infiltrated membrane (Figs. 1 and 2). Scattered diplococci were found also in the adjacent lymph follicles and in the peritoneal coat. In the lumen there were also a few gram-negative bacilli resembling colon bacilli, and what appeared to be fusiform bacilli. Cultures from a swab of the tonsils sent me by Dr. Reed 10 days after the operation, showed a predominating number of green-producing streptococci, a few colo-

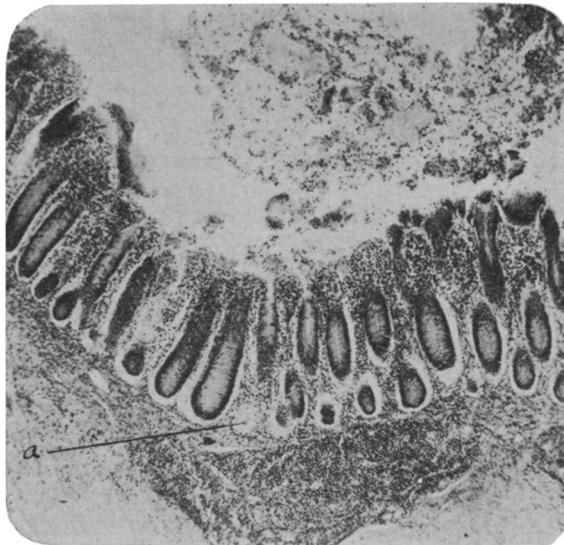


Fig. 1. Section of the appendix in human appendicitis. Note the sloughing of the mucous membrane, the hemorrhagic and leukocytic infiltration in the lymph follicle, the mucous membrane, and the submucosa. Hematoxylin and eosin.  $\times 75$ .

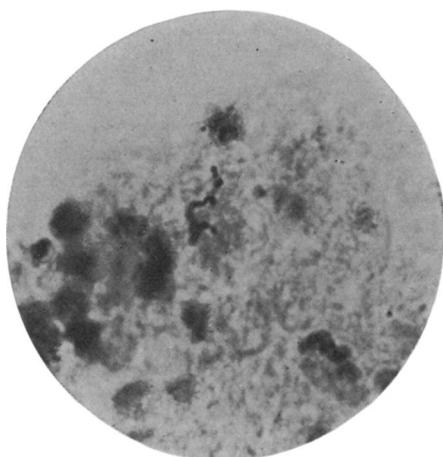


Fig. 2. Streptococci in submucosa at *a*, shown in Fig. 1. Gram-Weigert.  $\times 1200$ .

nies of hemolyzing streptococci, and a large number of colonies of *Micrococcus catarrhalis*. The broth culture revealed a pure growth of a short-chained streptococcus. Two rabbits were injected with the latter culture, one of which showed hyperemia and hemorrhages in the mucous membrane and the peritoneal coat of the appendix. It also showed a few hemorrhages in the tricuspid valve. The other rabbit showed only a slightly turbid joint fluid. Cultures from the blood of both on blood-agar plates disclosed pure growths of green-producing streptococci. The emulsion of one of the areas of hemorrhage in the peritoneal coat of the appendix showed many green colonies of streptococci.

On June 4 cultures from the tonsils were made again. The tonsils were larger than normal but not badly infected. The culture in ascites dextrose broth was injected into one rabbit; it developed a number of small hemorrhages in the appendix with hyperemia and edema, as well as a marked hemorrhagic edema of the parotid and associated lymph glands. There were also a number of hemorrhages in the muscles, particularly in the adductors of the thighs. The localization in the parotid is of interest, especially since this individual was the janitor in the hospital in which the patients with parotitis were treated and hence may be considered a possible carrier.

TABLE 1  
LOCALIZATION OF STREPTOCOCCI FOLLOWING INTRAVENOUS INJECTION

Sources of Streptococci		Time of Experiments	Animals	Strains	Percentage of Animals Showing Lesions in	
					Appen-	Paro-
Tonsils	Normal individuals	Soon after epidemic of appendicitis (March)	49	43	30	10
	Individuals that had had appendicitis	Soon after epidemic of appendicitis (March)	30	30	6	20
Dairy products.....		Soon after epidemic of appendicitis (March)	19	4	47	0
		Soon after epidemic of appendicitis (March)	22	9	41	9
		During epidemic of parotitis (March and April)	28	8	0	29
Steno's duct in parotitis.....		Soon after epidemic of parotitis (June)	10	6	0	30
		During epidemic of parotitis (March and April)	19	9	15	73

Table 1 gives a summary of the results following intravenous injection of streptococci isolated from tonsils, dairy products, and Steno's ducts. It is seen that the cultures obtained from the tonsils of normal individuals soon after the epidemic of appendicitis and at the beginning of the epidemic of parotitis produced lesions of the appendix in 30%, and in the parotid gland in 10% of the animals injected. After the epidemic of parotitis, cultures made in exactly the same way produced lesions in the appendix in 6% and in the parotid in 20% of the animals injected. The lesions in the appendix here correspond with the average

incidence of lesions in the appendix (5%) following injection of streptococci from a wide range of sources.<sup>8</sup> The cultures made soon after the epidemic of appendicitis from the tonsils in individuals who had had appendicitis produced this disease in 47% of the animals injected and no lesions in the parotid. Strains isolated from the dairy products soon after the epidemic of appendicitis, including cultures up to March 19, produced lesions in the appendix in 41%, and in the parotid in 9% of the animals injected; while during and soon after the epidemic of parotitis the strains failed to produce appendicitis, but produced parotitis in 29 and 30%, respectively, of the animals injected. The streptococci obtained from patients having parotitis during the epidemic produced lesions in the appendix in 15%, and in the parotid in 73% of the animals injected.

In this connection it should be noted that 4 of the 6 individuals whose tonsils were cultured and who had to do with the serving of food, including the waiter at the table at which 2 cadets developed appendicitis on the same day, showed streptococci having affinity for the appendix of rabbits. One of them is subject to repeated mild attacks of appendicitis.

The average incidence of lesions in the various organs and the rate of mortality in animals injected with cultures from the tonsils or the throats of 46 normal individuals during March was 14 and 41%, respectively; while during June they were only 8 and 33%, respectively. The evidence of infection in the tonsils was distinctly greater during March, altho none of the individuals complained of sore throat and in none was the inflammation acute. The occurrence of lesions was more frequent in the animals injected with cultures from distinctly infected tonsils (18%) than in animals injected with cultures from more normal tonsils, or normal throats (4) in which there had been a previous tonsillectomy (10%). Likewise, there was a distinctly higher incidence of lesions and a greater rate of mortality following injection of streptococci from the dairy products during March and April (11 and 26%, respectively) than during June (8 and 10%, respectively). These findings suggest that the seasonal prevalence of streptococcal throat infections is largely due to an increase in infective power of the streptococci in tonsils and possibly in dairy products as well.

It must not be supposed that the lesions in the appendix and the parotid are merely accidental. Cultures from the milk and the cream produced lesions in the appendix on March 6 and 19 while those

<sup>8</sup> Rosenow: Jour. Am. Med. Assn., 1915, 65, p. 1687.

injected on March 13, April 25, and June 4 failed entirely to produce lesions. In only one rabbit did the cultures from the milk and the cream produce parotitis (March 12). Cultures from the butter, made on March 5 and 13 and on April 9 and 25 and June 4 did not produce lesions in the appendix in rabbits, but did produce lesions in the parotid. Cultures from samples of butter obtained on April 9 showed a large number of 2 types of colonies of streptococci: the one produced distinct green colonies on blood agar; the other produced smaller, grayish, elevated, round colonies surrounded by a narrow hazy zone of hemolysis. Injections of the mixture produced marked edema and hemorrhage of the parotid in 2 rabbits. Pure cultures from the latter (second culture) produced marked edema and hemorrhage of the parotid in 2 of 3 rabbits. The strain which grew in pure culture in dextrose broth produced similar lesions in 2 rabbits, and after injection into Steno's duct in each of 3 dogs produced the swelling and cellular infiltration considered characteristic of mumps. (The results of the experiments with the organism from parotitis, which closely resembled the organism described by Herb,<sup>9</sup> will be detailed in a separate paper.) The cultures from the cream and the ice cream supplied at the neighboring shop produced marked lesions of the appendix in 2 rabbits injected March 19, while cultures on two subsequent occasions after the plant was remodeled failed to produce either appendicitis or parotitis. Cultures from the cheese failed to produce either appendicitis or parotitis on March 15, but produced appendicitis on March 13, and parotitis on April 25 and on June 4. Cultures made May 7 and June 4 from butter and ice cream from another source failed to produce either appendicitis or parotitis. Investigation showed that in the communities where the butter and the cheese were manufactured mumps was present in epidemic form during April and May—the time during which parotitis was so prevalent at the academy and during which there were found in the butter and the cheese streptococci having such marked affinity for the parotid gland. The possibility of infection of the butter and the cheese with these strains at the academy is excluded because the cultures were made from the original packages; but whether these strains were from human sources or were from the udders of cows it is impossible to say. It might be said, however, that the fermentative powers of some of the strains having affinity for the appendix suggest the latter origin, while those of strains producing the parotitis suggest the former source.

<sup>9</sup> Arch. Int. Med., 1909, 4, p. 201.

The cultures from the dairy products showed a preponderance of non-hemolyzing, short-chain-producing streptococci, often in almost pure form and in enormous numbers. Slightly hemolyzing streptococci were found occasionally. All were of a relatively low grade of virulence, but those producing parotitis caused death more frequently than did those producing appendicitis.

The importance of the streptococci contained in the dairy products as a possible source of infection for man is further shown by the fact that 6% of the animals injected showed ulcer of the stomach, 6% cholecystitis, 28% arthritis, 6% endocarditis, 20% myocarditis, and 26% myositis. The high incidence of myositis and myocarditis, which occurred 2 and 5 times as often as they occur with streptococci from the tonsils, is of special interest and in accord with the findings of Rosenow and Moon,<sup>10</sup> who showed that streptococci from milk during an epidemic of sore throat had a marked affinity for the muscles in animals.

The lesions other than those in the appendix and the parotid following injection of streptococci from the tonsils parallel very closely indeed those obtained previously by one of us<sup>11</sup> with streptococci from similar sources. It is realized of course that in man liability to infection following ingestion of the streptococci is less than it is in animals following intravenous injection. Yet, that infection may occur must be conceded.

The normal individuals during (10%), and immediately after (20%), the epidemic who harbored streptococci having elective affinity for the parotid in animals, must be regarded as carriers.

It would appear, then, that these epidemics of appendicitis and parotitis were due to streptococci contained in dairy products. This fact and the fact that milk is such an excellent culture medium make efficient pasteurization, or some other means of destroying the pathogenic bacteria which may be present in milk, imperative in order that the public health may be safeguarded.

<sup>10</sup> Jour. Infect. Dis., 1915, 17, p. 69.

<sup>11</sup> Rosenow: Ibid., 1912, 11, p. 338.